PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 502895	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT/AU2004/001456**	International filing date *(day/month/year)* 22 October 2004	Priority date *(day/month/year)* 24 October 2003
International Patent Classification (IPC) or national classification and IPC **Int. Cl.**[7] G01N 33/68; A61K 31/00		
Applicant IMMUNAID PTY LTD et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of **6** sheets, as follows:
      - [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand 4 August 2005	Date of completion of the report 27 September 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **ROSS A. OSBORNE** Telephone No. (02) 6283 2404

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/001456

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **1-46** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☒ the claims:

pages as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **47-52** received by this Authority on **4 August 2005** with the letter of 4 August 2005
pages* received by this Authority on with the letter of

☒ the drawings:

pages **1/13-13/13** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1-44**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims **1-44**	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims **1-44**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1: WO 2002/013828
D2: WO 2003/068257
D3: North, R. J. and Awward A. (1990) *Immunology* 71: 90-95
D4: Plana, M. *et al.* (2000) *AIDS* 14: 1921-1933
D5: WO 2001/008702
D6: US 6107020

Novelty (N)

The claims meet the criteria set forth in PCT Article 33(2) for novelty. The prior art published before the priority date does not disclose the methods comprising analysing effector cell and/or regulator cell cycling as defined in the claims.

Inventive Step (IS)

The claimed invention is not obvious in the light of any of the cited documents nor is it disclosed in any obvious combination of them. It is also considered that it would not be obvious to a person skilled in the art in the light of common general knowledge either by itself or in combination with any of these documents. Therefore the subject matter of these claims is not obvious and meets the requirements of Article 33(3) PCT with regard to inventive step.

CLAIMS

1. A method for analysing effector cell and/or regulator cell cycling to determine when an agent should be administered to a patient suffering from a disease characterized by the production of regulator cells, the method comprising monitoring the patient, or samples obtained therefrom, for at least one of: a) effector cell numbers and/or activity, b) regulator cell numbers and/or activity, c) a molecule associated with the disease, and/or d) an immune system marker.

2. A method of treating a disease characterized by the production of regulator cells, the method comprising;

i) analysing effector cell and/or regulator cell cycling by monitoring a patient suffering from the disease for at least one of:

a) number and/or activity of regulator cells,

b) number and/or activity of effector cells,

c) a molecule associated with the disease, and/or

d) an immune system marker, and

ii) exposing the patient to an agent to treat the disease,

wherein the timing of administration of the agent is selected such that the activity of effector cells is not significantly reduced.

3. The method of claim 1 or claim 2, wherein the disease characterized by the production of regulator cells is cancer or an infection.

4. The method of claim 3, wherein the infection is a chronic persistent infection characterized by the patient's immune system not being able to eliminate the infection.

5. The method of claim 4, wherein the patient is infected with HIV, Hepatitis B virus or Hepatitis C virus.

6. The method according to any one of claims 1 to 5, wherein the immune system marker reflects the number and/or activity of regulator cells, and/or the number and/or activity of effector cells.

7. The method according to any one of claims 1 to 5, wherein the immune system marker is an acute phase inflammatory marker.

8. The method of claim 7, wherein the acute phase inflammatory marker is selected from the group consisting of: serum amyloid A, serum amyloid P and c-reactive protein.

9. The method according to any one of claims 2 to 5, wherein the agent is administered between when the levels of an acute phase inflammatory marker have peaked and before the marker begins to rise in the next cycle.

10. The method according to any one of claims 1 to 9, wherein the regulator cells are CD4+CD8- T cells.

11. The method according to any one of claims 2 to 5, wherein the agent is administered about when CD4+CD8- T cells are detected.

12. The method according to any one of claims 1 to 11, wherein the effector cells are CD8+CD4- T cells.

13. The method according to any one of claims 2 to 5, wherein the agent is administered approximately when CD8+CD4- T cell numbers have peaked.

14. The method according to any one of claims 1 to 13, wherein the molecule associated with the disease is an antigen produced by a cancer cell or an infectious agent.

15. The method according to any one of claims 2 to 5, wherein the agent is administered approximately when levels of the molecule associated with the disease begin to decrease.

16. The method according to any one of claims 1 to 5, wherein the patient is monitored for an acute phase inflammatory marker, and a molecule associated with the disease.

17. The method according to any one of claims 2 to 5 or 16, wherein the agent is administered between when the levels of the acute phase inflammatory marker have peaked and before the marker begins to rise in the next cycle, and when levels of the molecule associated with the disease begin to decrease or would have been predicted to begin to decrease based upon previous analysis of the molecule.

18. The method according to any one of claims 1 to 17, wherein the patient is monitored for a period of at least 21 days.

19. The method according to any one of claims 1 to 18, the patient is monitored at least about every 3 days.

20. The method according to any one of claims 1 to 19, wherein the agent inhibits the production of, limits the function of, and/or destroys, regulator cells.

21. The method of claim 20, wherein the agent is selected from the group consisting of anti-proliferative drugs, radiation, dsRNA and antibodies which inhibit the production and/or activity of regulator cells.

22. The method of claim 21, wherein the anti-proliferative drug is selected from the group consisting of: taxol, vincristine, vinblastine and anhydro vinblastine.

23. The method of claim 21, wherein the antibody is selected from the group consisting of: anti-CD4+, anti-CTLA-4 (cytotoxic lymphocyte-associated antigen-4), anti-GITR (glucocorticoid-induced tumour necrosis factor receptor), anti-CD28 and anti-CD25.

24. The method according to any one of claims 1 to 23, wherein the patient has not been exposed to a treatment for the disease for at least 21 days.

25. The method according to any one of claims 1 to 24, wherein the patient is a human.

26. A method for analysing effector cell and/or regulator cell cycling to diagnose a disease characterized by the production of regulator cells, the method comprising monitoring the patient, or samples obtained therefrom, for at least one of: a) effector cell numbers and/or activity, b) regulator cell numbers and/or activity, c) a molecule associated with the disease, and/or d) an immune system marker, wherein cycling of any one of a) to d) indicates the disease may be present.

27. A method for analysing effector cell and/or regulator cell cycling to determine when a vaccine should be administered to a patient suffering from a disease characterized by the production of regulator cells, the method comprising monitoring the patient, or samples obtained therefrom, for at least one of: a) effector cell numbers

and/or activity, b) regulator cell numbers and/or activity, c) a molecule associated with the disease, and/or d) an immune system marker.

28. A method of treating a disease characterized by the production of regulator cells, the method comprising;

i) analysing effector cell and/or regulator cell cycling by monitoring a patient suffering from the disease for at least one of:

a) number and/or activity of regulator cells,

b) number and/or activity of effector cells,

c) a molecule associated with the disease, and/or

d) an immune system marker, and

ii) exposing the patient to an vaccine to treat the disease,

wherein the timing of administration of the vaccine is selected such that the activity of effector cells is not significantly reduced.

29. The method of claim 28, wherein the vaccine is administered about when the levels of effector cells are increasing.

30. The method of claim 28, wherein the vaccine is administered about when the levels of a molecule associated with the disease begin to decrease.

31. The method of claim 28, wherein the vaccine is administered about when the levels of an acute phase inflammatory marker begin to increase.

32. Use of an assay which detects an immune system marker for analysing effector cell and/or regulator cell cycling to determine when an agent or vaccine should be administered to a patient suffering from a disease characterized by the production of regulator cells.

33. The use of claim 32, wherein the marker is an acute phase inflammatory marker.

34. The use of claim 33, wherein the acute phase inflammatory marker is selected from the group consisting of: serum amyloid A, serum amyloid P and c-reactive protein.

35. Use of an assay which detects effector cell numbers and/or activity for analysing effector cell and/or regulator cell cycling to determine when an agent or

vaccine should be administered to a patient suffering from a disease characterized by the production of regulator cells.

36. The use of claim 35, wherein the assay detects the number of CD8+CD4- T cells.

37. Use of an assay which detects regulator cell numbers and/or activity for analysing effector cell and/or regulator cell cycling to determine when an agent or vaccine should be administered to a patient suffering from a disease characterized by the production of regulator cells.

38. The use of claim 37, wherein the assay detects the number of CD4+CD8- T cells.

39. Use of an assay which detects a molecule associated with a disease characterized by the production of regulator cells for analysing effector cell and/or regulator cell cycling to determine when an agent or vaccine should be administered to treat the disease.

40. The use of claim 39, wherein the assay detects an antigen produced by a cancer cell or an infectious agent.

41. The use according to any one of claims 32 to 40, wherein a patient with the disease has not been exposed to a treatment for the disease for at least 21 days.

42. Use of an agent for the manufacture of a medicament for administering to a patient suffering from a disease characterized by the production of regulator cells, wherein the agent will be administered at a time selected such that the activity of effector cells is not significantly reduced, and wherein the patient has not been exposed to a treatment for the disease for at least 21 days.

43. The use according to any one of claims 32 to 42, wherein the agent inhibits the production of, limits the function of, and/or destroys, regulator cells.

44. A kit when used for analysing effector cell and/or regulator cell cycling to determine when an agent or vaccine should be administered to a patient suffering from a disease characterized by the production of regulator cells, the kit comprising at least one reagent for monitoring the patient, or samples obtained therefrom, for at

least one of: a) effector cell numbers and/or activity, b) regulator cell numbers and/or activity, c) a molecule associated with the disease, and/or d) an immune system marker.